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10/082,122	02/26/2002	Philippa Radcliffe	078883-0145	5398

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,122	RADCLIFFE ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is an original application filed February 26, 2002, which claims benefit to foreign applications 0130797.4 filed December 21, 2001 and 0201140.1 filed January 18, 2002 in the United Kingdom.

Claims 1-25 are pending.

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on July 26, 2004 is acknowledged. The traversal is on the ground(s) that the claimed methods do not make different products and can be sued to make either a cell or a transgenic animal. Further, it is argued that there would not be an undue burden to examine all the groups together. This is found persuasive in part because the claimed products can be made by any of the different methods known in the prior art, and thus a complete search would require a different search and examination than that required for the claimed methods.. In particular it is noted that the specification contemplates both making transgenic organisms and using the system for gene therapy which comprise very different areas of the art. However, Examiner would agree that the instantly claimed inventions would not be an undue burden to examine together.

The restriction requirement is withdrawn.

Claims 1-25 are pending and currently under examination.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), filed June 6, 2002, which papers have been placed of record in the file.

Oath/Declaration

This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. Specifically, a preliminary amendment was filed February 26, 2002, however subsequently the executed declaration filed June 6, 2002 does not reflect that this preliminary amendment was made or reviewed. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 24 and 25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to 'transgenic organisms'. As written in light of the teachings of the instant specification the claimed cells read on a transgenic human being. A human being or human embryo is not-statutory subject matter. See 1077 O.G. 24, April 21, 1987.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13, 15-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of using non-primate lentiviral vectors in mammalian cells, does not reasonably provide enablement for use of such vectors in non-mammalian cells encompassed by other animals, yeast (claims 12 and 15), *C. elegans* nor drosophila (claim 16). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

At the time of filing the use of non-primate lentiviral vectors where known and used to infect a variety of cell types *in vitro* and *in vivo* (see for example Mitrophanous *et al.* or Kingsman *et al.*) however, it was generally recognized that the genomic differences among lentiviral vectors would require empirical characterization of each vector system for its use in any specific cell (Olsen , 2001). For example any particular vector can only infect a cell for which it can specifically bind and infect, *i.e.* the target cell has the appropriate cell surface protein that allows for infection of the lentivirus. Moreover, the replication machinery of the lentivirus requires specific host cells to effectively express, replicate and package the viral genome. At the time of filing and presently, there is no evidence in the art that non-mammalian cells such as yeast, flies, *C. elegans*, recited and encompassed by the instant claims are capable for use in the instantly claimed methods. The present specification simply sets forth that the method could be used in non-mammalian cell types however, provides no specific teaching nor working example that such cells are capable of working in the methods as claimed. Based on the unpredictability of the lentiviral vectors recognized in the art at the time of filing, the basic biological requirements of the host cell in which they are present, and the lack of any specific teaching on how to modify the lentivirus or the non-mammalian host cell, it would require undue experimentation to practice the methods as broadly claimed. The high degree of unpredictability associated with the claimed method underscores the need to provide teachings in the specification that would provide the artisan with specific methodology to practice the claimed

method in all the cell types and organisms encompassed by the claims. Without such guidance in the specification and the lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan. The instant portion of the invention, as claimed, falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genentech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005). The claimed methods of transfer constitute such a "germ of an idea".

The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel.* In the instant case, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically,

The recitation of nucleotide of interest is vague and indefinite. What an artisan might define of interest is subject to change among individuals. The metes and bounds of the claims can not be specifically defined because the term 'interest' is relative and subjective depending on the artisan. It is unclear if claim 1 encompasses infecting any cell with FIV, if for example the artisan were interested in studying the transmission and pathology of FIV in cats or into a humans.

Claim 8 is vague and unclear in the recitation of "the cell is capable of giving rise to a germ line change" because 'capable' would depend on how one were to interpret how the cell is used. For example one may consider any cell capable of contributing to germ line change because the availability of nuclear transfer methodology. More clearly setting forth cell type related to its claimed capability would address the basis of the rejection.

Claim 20 is unclear and confusing on how the non-primate lentiviral vector "is an antisense oligonucleotide" as recited in the claim. Amending the claim to encompass encoding an antisense would address the basis of the rejection.

Claim 24 is confusing because claim 1 is drawn to a method not a cell, therefore it is unclear what cell claim 1 defines for that is used to generate the transgenic organism of claim 24.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 5-8, 11-15, 17-25 are rejected under 35 U.S.C. 102(a/e) as being anticipated by Kingsman *et al.* (IDS reference).

The applied reference has a common assignee and one common inventor (Mitrophanous) with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Kingsman *et al.* teach non-primate lentiviral vectors and there use for the delivery of a transgene to a cell *in vitro* and *in vivo*. Kingsman *et al.* teach that the genomes of the vectors can be modified and used to infect a wide variety of mammalian cell types for the expression any product that can be encoded by a polynucleotide.

Claims 1-3, 8, 12-15, 17-21, 23, 24 and 25, are rejected under 35 U.S.C. 102(b) as being anticipated by Mitrophanous *et al.* (Gene Therapy, 1996).

Mitrophanous *et al.* teach methods for the stable transfer of non-primate lentiviral vectors into the nervous system of a rat. More specifically, Mitrophanous *et al.* found that pol dUTPase activity is not required and that they can be adapted by pseudotyping with other envelopes to make vectors that provide an alternative to HIV based vectors. With respect to claims 24 and 25 it is noted that transgenic is broadly defined in the instant specification as an organism which includes in at least one of its cells a transgene (page 110, lines 5-16) so include an animal treated by gene therapy. In this case the treated rats expressing a detectable marker (see figure 6 for example) anticipate the claimed transgenic animals.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15, 17-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Readhead *et al.* (US Patent 6,734,338 B1) and Mitrophanous *et al.*

Readhead *et al.* teach methods of using lentiviral vectors to transfect and generate alterations to the germ cells of an animal (see for example claim 3). More specifically, by administering a lentiviral vector to a germ cell either *in vitro* or *in vivo*, a transgenic cell is generated that is capable of producing transgenic offspring. The types of transgenes that are contemplated for delivery and/or expression broadly encompass any polynucleotide , in particular sequences that can be used to study other gene function in the resulting animals (see for example column 11, lines 50-67). Readhead *et al.* teach the use of a pseudotyped lentiviral vector to affect the germ cells of the animal being affected by the methodology, however they do not teach specifically to use 'non-primate' lentiviral vectors. As discussed above, Mitrophanous *et al.* teach the potential problems recognized in the art for using primate based lentiviral vectors and provide the specific guidance for the use of non-primate lentivirus vectors. In addition, it should be noted that any particular lentviral vector would have specific characteristics that would make it beneficial for use in the species in which is normally found, for example EIAV for horses or CAEV for goats. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the detailed guidance of Mitrophanous *et al.* for the use of non-primate lentiviral vectors in the methods described by Readhead *et al.* because of the advantages of using lentiviral vectors specific for a particular non-primate species and for avoiding potential problems of HIV based lentiviral vectors recognized in the art. One having ordinary skill in the art would have been motivated to use the specific vectors and teachings of Mitrophanous *et al.* because of the art recognized problems for the use of other lentiviral vectors. There would have been a reasonable expectation of success given the working examples and results of Readhead *et al.* who demonstrate that germ cells can

be affected by lentiviral vectors and Mitrophanous *et al.* demonstrating that non-primate lentiviral vectors can be pseutotyped and used in methods for the delivery of a polynucleotide into a variety of cell types.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Humeau *et al.* US Patent 6,627,442 B1 disclose the use of lentiviral chimeric HIV-derived vectors and provide the necessary guidance for use of such vectors *in vitro* and *in vivo*.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach